REMARKS

Claims 8, 10-14, and 18-43 were pending in the application. New claims 44-48 have been added. Following entry of this Amendment and Response, claims 8, 10-14, and 18-48 will be pending in the instant application.

Support for new claims 44-48 can be found throughout the specification and claims as originally filed. No new matter has been added.

Interview Summary

Applicants and Applicants' attorneys gratefully acknowledge the personal interview between Elizabeth Hanley and Cristin Cowles, Applicant's attorneys, and Examiner David Blanchard on July 14, 2009. In the interview, the obviousness rejection of record was discussed.

Rejection of Claims 8, 10-14, 18-26, and 28-43 Under 35 U.S.C. § 103(a)

The rejection of claims 8, 10-14,18-26, and 28-43 under 35 U.S.C. § 103(a) as being obvious in view of Oh *et al.* (Journal of the American Academy of Dermatology, 42(5):829-830, 2000) in combination with Salfeld *et al.* ([a] WO 97/29131 or [b] U.S. Patent No. 6,509,015 B1; collectively referred to as "Salfeld" below), and Keystone *et al.* ("The Fully Human Anti-TNF Monoclonal Antibody, Adalimumab (D2E7), Dose Ranging Study: The 24-Week Clinical Results in Patients with Active RA on Methotrexate Therapy (The ARMADA Trial)," *Presented at the Annual Meeting of the European League Against Rheumatoid Arthritis (EULAR), Prague, Czech Republic,* June 2001) has been maintained (see pages 3-7 and page 8 of Office Action dated June 17, 2009). Applicants respectfully disagree and traverse the rejection.

Each of claims 8, 10-14,18-26, and 28-43 requires *subcutaneous administration* of a dosage of a *human anti-TNFα antibody, or an antigen-binding fragment thereof*, for the treatment of *psoriasis,* whereby the dosage of the antibody, or antigen binding portion thereof, *comprises 10-150 mg and is the same dosage throughout the course of treatment.* Claims 8, 10-14, and 18-34 further require *biweekly* administration of the antibody, or antigen binding portion thereof. New

claims 44-48 require *subcutaneous administration* of a dosage of a *human anti-TNFα antibody, or an antigen-binding fragment thereof*, for the treatment of *psoriasis,* whereby the dosage of the antibody, or antigen binding portion thereof, *consists of 10-150 mg.*

Oh *et al.* is used as the primary reference, and is cited for teaching the use of a chimeric antibody to treat psoriasis. The Examiner suggests that one of ordinary skill would be motivated to essentially replace the chimeric antibody of Oh *et al.* with the human TNFa antibody described in Salfeld based on the teachings of Salfeld with respect to unwanted immune reactions associated with chimeric antibodies (due to the presence of murine sequences). Finally, the Examiner relies upon Keystone to provide the dosing regimen recited in the claims, suggesting that "common sense and ordinary skill would have led the ordinary skilled artisan to follow a known dosing regimen for the antibody to be used in therapy." Applicants respectfully disagree.

Applicants submit that one of ordinary skill would not have been able to predict with a reasonable expectation of success that human TNFa antibodies, or antigen-binding portions thereof, would be effective at treating psoriasis based on the teachings of Oh *et al.* directed to infliximab. Furthermore, neither Salfeld nor Keystone teach or suggest that a human TNFa antibody, or antigen binding portion thereof, would be effective at treating psoriasis. The Examiner suggests that one of ordinary skill would have looked to the dosing regimen of Keystone based on "common sense," rather than looking to the dosing regimen of Oh *et al.* Applicants respectfully submit, however, that given that the dosing regimen of infliximab is not the same for rheumatoid arthritis and psoriasis (explained in detail in Applicants' previous responses), "common sense" would have led one of ordinary skill to a different regimen than that described in Keystone. Thus, Applicants respectfully submit that one of ordinary skill in the art would not have had an expectation of success in combining the cited references to arrive at the claimed invention.

The Examiner suggests that the claimed invention is a "recognized results-effective variable" based on the teachings of Salfeld, and cites *In re Antonie*, 559 F.2d 618, 195 USPQ 6 and *In re Aller*, 220 F.2d 454, 456 (see also MPEP 2144.05). Notably, MPEP 2144.05 II.B, referenced by the Examiner, is entitled "Obviousness of ranges / Optimization of ranges / Only result-effective variables can be optimized."

Applicants respectfully submit that the claimed invention is not an alteration of a range, as suggested by the citation to the MPEP. Rather the invention relates to the discovery that human TNFa antibodies, or antigen-binding portions thereof, may be used to treat psoriasis.

Applicants respectfully note that the comparison of the claimed invention to the facts of *In re Aller* is not on point, as the claimed invention is not a mere optimization of a known process. The invention at issue in *In re Aller* was a process which was "identical with that of the prior art" except for the alteration of a temperature and ingredient concentration amount (*In re Aller*, 220 F.2d 454). The court held in *In re Aller* that the "claimed process [was] merely different in degree and not in kind from the reference process," and maintained the claimed invention as obvious over the cited reference.

Applicants' invention is based on the discovery that a human TNFα antibody, or antigen-binding portion thereof, may be used to treat psoriasis via subcutaneous administration to a subject in need thereof at a dose comprising 10-150 mg. The primary reference, Oh *et al.*, teaches the use of a chimeric antibody via infusion at a weight-based dose of 5 mg/kg. Taking the method of Oh *et al.* as the "known process" to which the Examiner is comparing Applicants' invention, the claimed invention is *not* an optimization of the parameters described in the cited reference, as the methods of treatment of the claimed invention and Oh *et al.* share a common disease (psoriasis), but differ in the type of treatment (fixed dose vs. weight-based dosing), the type of therapeutic agent (human vs. chimeric TNFα antibody), and the mode of administration (subcutaneous vs. infusion). Moreover, claims 8, 10-14,18-26, and 28-43 also differ in the dosing schedule in comparison to Oh *et al.* Indeed, the Examiner relies upon two other references to make up for these deficiencies, including Keystone *et al.* for teaching a fixed dose. As such, the claimed invention is not an optimization of a known process, *i.e.,* the method of Oh *et al.*

Applicants re-iterate that the Examiner has failed to establish how the claimed methods were selected from a finite number of identified, predictable solutions, as required under the guidelines set forth under MPEP § 2143 (E) for establishing obviousness under the "obvious to try" rationale. Dosage amounts alone or in combination with a dosing schedule provide an infinite number of possible

combinations for treatment. There exists a limitless number of dosage amounts that can be used in any given treatment, as there also exists a limitless dosing schedule in terms of how frequently an agent may be delivered. Accordingly, the combination of dose amounts and frequency is equally infinite.

In addition, Applicants respectfully wish to clarify the Examiner's suggestion that the arguments filed 4/14/08, 11/3/08, and 4/13/09 are inconsistent, with respect to the teachings of Oh *et al.* The remarks described in Applicants' response filed on 4/14/08 and quoted by the Examiner were made in context of describing the mode of administration and dose amounts described in Oh *et al.* Similarly, the remarks described in Applicants' response filed on 11/3/08 and quoted by the Examiner were also made in the context of describing the mode of administration and dose amounts described in Oh *et al.* In each instance, Applicants comments were not directed to whether or not the teachings of Oh *et al.* were successful, but rather Applicants were contrasting that the dose amounts and mode of administration of Oh *et al.* are not equivalent to the claimed invention (at the time of each rejection), *i.e.,* biweekly, subcutaneous administration of a dose comprising 10-150 mg of a TNFa antibody. Remarks made in both the 4/14/08 and 11/3/08 responses are consistent with the teachings of Oh *et al.* as described at page 829, second column, lines 9-19. Furthermore, with respect to the Examiner's suggestion that Applicants characterized the results in Oh *et al.* as "dramatic," Applicants respectfully submit that the term "dramatic" was used with respect to how the reference itself, *i.e.*, Oh *et al.* described the results (see page 9, last paragraph of response dated 4/13/09).

In view of the above, Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection of Claims 8, 10, 12, and 27 Under 35 U.S.C. § 103(a)

Claims 8, 10, 12 and 27 are rejected as being unpatentable over Oh *et al.* (Journal of the American Academy of Dermatology, 42(5):829-830, 2000) in view of Salfeld *et al.* ([a] WO 97/29131 and Keystone *et al.* ("The Fully Human Anti-TNF Monoclonal Antibody, Adalimumab (D2E7), Dose Ranging Study: The 24-Week Clinical Results in Patients with Active RA on Methotrexate Therapy (The

ARMADA Trial)," *Presented at the Annual Meeting of the European League Against Rheumatoid Arthritis (EULAR), Prague, Czech Republic,* June 2001) and Neuner *et al.* (Photochem. Photobiol 59(2):182, Feb. 1994) on the ground that it would have been *prima facie* obvious to one of ordinary skill in the art to arrive at the claimed methods of treating psoriasis, in view of the combined teachings of the cited references. Applicants respectfully disagree and traverse the rejection.

As argued above, the combined teachings of Oh *et al.*, Salfeld *et al.*, and Keystone *et al.* fails to establish a *prima facie* case of obviousness. While Neuner *et al.* describes PUVA therapy for treating psoriasis, the reference does not make up for the deficiencies described above. Accordingly, Applicants respectfully request that the rejection of the pending claims on the ground of obviousness be reconsidered and withdrawn.

Provisional Rejection of Claims for Non-Statutory Obviousness-Type Double Patenting

The *provisional* rejection of claims 8, 10-14, 18-26, and 28-43 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-10, 16-21, 78-79, 81, 84, 86-88, 95, 97-98, and 100-104 of copending Application No. 10/163,657 in view of Oh *et al.* was maintained. The Examiner has also maintained the *provisional* rejection of claims 8, 10-14, 18-25, and 28-43 as being unpatentable in view of claims 5, 9-22, 25-26, and 28-53 of copending Application No. 11/104,117 in view of Oh *et al.* Furthermore, claims 8, 10-14, 18-26 and 28-43 are *provisionally* rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claim 15 of copending Application No. 11/233,252 (allowed) in view of Oh *et al.* and Keystone *et al.*

Applicants note that these rejections are provisional in nature and respectfully submit that they will be further addressed when appropriate, *i.e.*, when the nonstatutory obviousness-type double patenting rejection is the only rejection remaining in the later-filed application (MPEP § 804 I.B.).

Applicants further note that Application No. 11/233,252 is now issued as US Patent No. 7588761. As argued above, the combined teachings of Salfeld *et al.*, Oh *et al.* and Keystone *et al.* fail to provide a reasonable expectation of success for the

treatment of psoriasis with a subcutaneous dosage regimen of a human anti-TNFα antibody as presently claimed.

Rejection of Claims for Non-Statutory Obviousness-Type Double Patenting

Claims 8, 10-14, 18-25 and 28-43 and are rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 1-7, 36-39 and 69-70 of U.S. Patent No. 6,509,015 B1, to Salfeld *et al.*, in view of Oh *et al.* and Keystone *et al.* Applicants respectfully disagree and traverse the rejection.

As argued above, the combined teachings of Salfeld *et al.*, Oh *et al.* and Keystone *et al.* fail to provide a reasonable expectation of success for the treatment of psoriasis with a subcutaneous dosage regimen of a human anti-TNFα antibody as presently claimed. Accordingly, Applicants respectfully request that the rejection of the pending claims on the ground of nonstatutory obviousness-type double patenting, be reconsidered and withdrawn.

SUMMARY

In view of the foregoing, Applicants believe that the application is now in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' Attorney at (617) 449-6550

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Respectfully submitted,

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